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RESPONSE UNDER 37 CFR 1.104

EXPEDITED PROCESSING

EXAMINING GROUP

**In the Claims**

Please amend claims 7, 9, 10, 13, 14 and 16 to read as follows.

D<sup>1</sup> 7. (Twice amended) A compound according to Claim 16 in which Ar<sup>2</sup> is a 1,4-phenylene group optionally substituted with one or two atoms or groups -L<sup>2</sup>(Alk)<sub>i</sub>L<sup>3</sup>(R<sup>4</sup>)<sub>u</sub>.

D<sup>2</sup> 9. (Twice amended) A compound according to Claim 16 in which Ar<sup>1</sup> is a pyrimidinyl, pyridyl or phenyl group optionally substituted with one or more atoms or groups -L<sup>2</sup>(Alk)<sub>i</sub>L<sup>3</sup>(R<sup>4</sup>)<sub>u</sub>.

10. (Amended) A compound according to Claim 9 in which Ar<sup>1</sup> is a pyridyl or phenyl group optionally substituted with one or more atoms or groups -L<sup>2</sup>(Alk)<sub>i</sub>L<sup>3</sup>(R<sup>4</sup>)<sub>u</sub>.

D<sup>3</sup> 13. (Amended) A compound according to Claim 12 in which R<sup>3</sup> is a pyrrolidinyl or thiazolidinyl group optionally substituted with one or more halogen atoms, C<sub>1-6</sub>alkyl groups, haloC<sub>1-6</sub>alkyl groups optionally substituted with one or more hydroxyl groups, hydroxyl groups, C<sub>1-6</sub>alkoxy groups, haloC<sub>1-6</sub>alkoxy groups, thiol groups, C<sub>1-6</sub>alkylthio groups, aromatic groups, heteroaromatic groups, or -(Alk<sup>2</sup>)<sub>v</sub>R<sup>10</sup> groups, and each nitrogen atom of the pyrrolidinyl or thiazolidinyl group is optionally substituted with a group -(L<sup>5</sup>)<sub>p</sub>(Alk<sup>3</sup>)<sub>q</sub>R<sup>12</sup>;

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or R<sup>3</sup> is a phenyl, pyrimidinyl or 1,3,5-triazinyl group optionally substituted with one or more atoms or groups -R<sup>13a</sup> or -Alk<sup>4</sup>(R<sup>13a</sup>)<sub>m</sub>.

14. (Amended) A compound which is:

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({4-[2-hydroxyethylamino]-6-methoxy-1,3,5-triazin-2-yl}amine)propanoic acid;

3-[(3,5-Dichloroisonicotinoyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)-amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2,6-dimethoxybenzoyl)amino]propanoic acid;

3-({[(4S)-3-Acetyl-1,3-thiazolinan-4-yl]carbonyl}amino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl}carbonyl)amino]propanoic acid;

(2RS,3RS)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl)carbonyl}amino]-2-hydroxypropanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2-[(2,5-dimethoxyphenyl)thio]-3-pyridinyl}carbonyl)amino]propanoic acid;

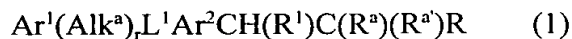
and the salts, hydrates and N-oxides thereof.

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EXAMINING GROUP 2500

1 To (Amended three times) A compound of formula (1):



wherein

$\text{Ar}^1$  is an aromatic or  $\text{C}_{1-9}$  heteroaromatic group containing one to four heteroatoms selected from oxygen, nitrogen, and sulfur, and is optionally substituted with one or more atoms or groups  $-\text{L}^2(\text{Alk})_t\text{L}^3(\text{R}^4)_u$ ;

$\text{L}^2$  and  $\text{L}^3$ , which may be the same or different, is each a covalent bond or a divalent linker atom or group selected from  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{O}-$ ,  $-\text{OC}(\text{O})-$ ,  $-\text{C}(\text{S})-$ ,  $-\text{S}(\text{O})-$ ,  $-\text{S}(\text{O})_2-$ ,  $-\text{N}(\text{R}^8)-$ ,  $-\text{CON}(\text{R}^8)-$ ,  $-\text{OC}(\text{O})\text{N}(\text{R}^8)-$ ,  $-\text{CSN}(\text{R}^8)-$ ,  $-\text{N}(\text{R}^8)\text{CO}-$ ,  $-\text{N}(\text{R}^8)\text{C}(\text{O})\text{O}-$ ,  $-\text{N}(\text{R}^8)\text{CS}-$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^8)-$ ,  $-\text{N}(\text{R}^8)\text{S}(\text{O})_2-$ ,  $-\text{N}(\text{R}^8)\text{CON}(\text{R}^8)-$ ,  $-\text{N}(\text{R}^8)\text{CSN}(\text{R}^8)-$ , and  $-\text{N}(\text{R}^8)\text{SO}_2\text{N}(\text{R}^8)-$ ;

$\text{R}^8$  is a hydrogen atom or a  $\text{C}_{1-6}$  alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or  $\text{C}_{1-6}$  alkoxy groups;

$t$  is zero or the integer 1;

$u$  is an integer 1, 2 or 3;

$\text{Alk}$  is an aliphatic or heteroaliphatic chain;

$\text{R}^4$  is a hydrogen or halogen atom or a group selected from  $\text{C}_{1-6}$  alkyl,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^6$ ,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{SO}_3\text{H}$ ,  $-\text{SO}_3\text{R}^5$ ,  $-\text{SOR}^5$ ,  $-\text{SO}_2\text{R}^5$ ,  $-\text{OCO}_2\text{R}^5$ ,  $-\text{CONR}^5\text{R}^6$ ,

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-OCONR<sup>5</sup>R<sup>6</sup>, -CSNR<sup>5</sup>R<sup>6</sup>, -COR<sup>5</sup>, -OCOR<sup>5</sup>, -N(R<sup>5</sup>)COR<sup>6</sup>, -N(R<sup>5</sup>)CSR<sup>6</sup>, -SO<sub>2</sub>N(R<sup>5</sup>)(R<sup>6</sup>),  
-N(R<sup>5</sup>)SO<sub>2</sub>R<sup>6</sup>, -N(R<sup>5</sup>)CON(R<sup>6</sup>)(R<sup>7</sup>), -N(R<sup>5</sup>)CSN(R<sup>6</sup>)(R<sup>7</sup>), and -N(R<sup>5</sup>)SO<sub>2</sub>N(R<sup>6</sup>)(R<sup>7</sup>); and

R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup>, which may be the same or different, is each a hydrogen atom or a straight or branched C<sub>1-6</sub>alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C<sub>1-6</sub>alkoxy groups;

provided that when t is zero and each of L<sup>2</sup> and L<sup>3</sup> is a covalent bond, then u is the integer 1 and R<sup>4</sup> is other than a hydrogen atom;

L<sup>1</sup> is a covalent bond or a linker atom or group selected from -CON(R<sup>2</sup>)-,

-S(O)<sub>2</sub>N(R<sup>2</sup>)-, -N(R<sup>2</sup>)-, and -O-;

R<sup>2</sup> is a hydrogen atom or a C<sub>1-3</sub> alkyl group;

Ar<sup>2</sup> is a phenylene group optionally substituted with one or two atoms or groups

-L<sup>2</sup>(Alk)<sub>t</sub>L<sup>3</sup>(R<sup>4</sup>)<sub>u</sub>;

R<sup>1</sup> is a group selected from -NHCOR<sup>3</sup>, -NHSO<sub>2</sub>R<sup>3</sup>, -NHR<sup>3</sup>, -NHC(O)OR<sup>3</sup>, -NHCSR<sup>3</sup>, -NHCON(R<sup>3</sup>)(R<sup>3a</sup>), -NHSO<sub>2</sub>N(R<sup>3</sup>)(R<sup>3a</sup>), and -NHCSN(R<sup>3</sup>)(R<sup>3a</sup>);

R<sup>3</sup> is an optionally substituted C<sub>3-10</sub> cycloaliphatic group, an optionally substituted C<sub>7-10</sub> polycycloaliphatic group, an optionally substituted C<sub>3-10</sub> heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-, -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-,

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-N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)- and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-; an optionally substituted C<sub>7-10</sub> heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-, -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-, -N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)- and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-; an optionally substituted aromatic group, or an optionally substituted C<sub>1,9</sub> heteroaromatic group containing one, two, three or four heteroatoms selected from oxygen, nitrogen, and sulfur;

R<sup>3a</sup> is a hydrogen atom, an optionally substituted C<sub>1,6</sub> aliphatic group, an optionally substituted C<sub>1,6</sub> heteroaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-, -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-, -N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)- and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-, an optionally substituted C<sub>3-10</sub> cycloaliphatic group, an optionally substituted C<sub>7-10</sub> polycycloaliphatic group, an optionally substituted C<sub>3-10</sub> heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-, -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-, -N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)- and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-; an optionally substituted C<sub>7-10</sub> heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-,

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EXPTD. IN PROSECUTION

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*Q* -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-,  
 -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-, -N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)- and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-; an  
 optionally substituted aromatic group, or an optionally substituted C<sub>1-9</sub> heteroaromatic group  
 containing one, two, three or four heteroatoms selected from oxygen, nitrogen, and sulfur;

wherein the optional substituents for the aromatic groups and the heteroaromatic  
 groups of R<sup>3</sup> and R<sup>3a</sup> are selected from one or more atoms or groups R<sup>13</sup> wherein R<sup>13</sup> is -R<sup>13a</sup> or  
 -Alk<sup>4</sup>(R<sup>13a</sup>)<sub>m</sub>;

R<sup>13a</sup> is a halogen atom, or an amino, substituted amino, nitro, cyano, amidino,  
 hydroxyl, substituted hydroxyl, formyl, carboxyl, esterified carboxyl, thiol, substituted thiol,  
 -COR<sup>14</sup>-, -CSR<sup>14</sup>-, -SO<sub>3</sub>H-, -SOR<sup>14</sup>-, -SO<sub>2</sub>R<sup>14</sup>-, -SO<sub>2</sub>NH<sub>2</sub>-, -SO<sub>2</sub>NHR<sup>14</sup>-, -SO<sub>2</sub>N(R<sup>14</sup>)<sub>2</sub>-, -CONH<sub>2</sub>-,  
 -CSNH<sub>2</sub>-, -CONHR<sup>14</sup>-, -CSNHR<sup>14</sup>-, -CON(R<sup>14</sup>)<sub>2</sub>-, -CSN(R<sup>14</sup>)<sub>2</sub>-, -N(R<sup>11</sup>)SO<sub>2</sub>R<sup>14</sup>-, -N(SO<sub>2</sub>R<sup>14</sup>)<sub>2</sub>-,  
 -N(R<sup>11</sup>)SO<sub>2</sub>NH<sub>2</sub>-, -N(R<sup>11</sup>)SO<sub>2</sub>NHR<sup>14</sup>-, -N(R<sup>11</sup>)SO<sub>2</sub>N(R<sup>14</sup>)<sub>2</sub>-, -N(R<sup>11</sup>)COR<sup>14</sup>-, -N(R<sup>11</sup>)CONH<sub>2</sub>-,  
 -N(R<sup>11</sup>)CONHR<sup>14</sup>-, -N(R<sup>11</sup>)CON(R<sup>14</sup>)<sub>2</sub>-, -N(R<sup>11</sup>)CSNH<sub>2</sub>-, -N(R<sup>11</sup>)CSNHR<sup>14</sup>-, -N(R<sup>11</sup>)CSN(R<sup>14</sup>)<sub>2</sub>-,  
 -N(R<sup>11</sup>)CSR<sup>14</sup>-, -N(R<sup>11</sup>)C(O)OR<sup>14</sup>-, -SO<sub>2</sub>NHet<sup>1</sup>-, -CONHet<sup>1</sup>-, -CSNHet<sup>1</sup>-, -N(R<sup>11</sup>)SO<sub>2</sub>NHet<sup>1</sup>-,  
 -N(R<sup>11</sup>)CONHet<sup>1</sup>-, -N(R<sup>11</sup>)CSNHet<sup>1</sup>-, -SO<sub>2</sub>N(R<sup>11</sup>)Het<sup>2</sup>-, -Het<sup>2</sup>-, -CON(R<sup>11</sup>)Het<sup>2</sup>-, -CSN(R<sup>11</sup>)Het<sup>2</sup>-,  
 -N(R<sup>11</sup>)CON(R<sup>11</sup>)Het<sup>2</sup>-, -N(R<sup>11</sup>)CSN(R<sup>11</sup>)Het<sup>2</sup>-, aryl or heteroaryl group;

R<sup>14</sup> is an -Alk<sup>4</sup>(R<sup>13a</sup>)<sub>m</sub>, aryl or heteroaryl group;

NHet<sup>1</sup> is a C<sub>3-7</sub>-cyclicamino group optionally containing one or more -O- or -S-  
 atoms or -N(R<sup>11</sup>)-, -C(O)- or -C(S)- groups and optionally substituted with one or more  
 substituents as defined for the cycloaliphatic groups of R<sup>3</sup> and R<sup>3a</sup>;

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EXAMINING GROUP 1649

D4  
Het<sup>2</sup> is a monocyclic C<sub>5-7</sub> carbocyclic group optionally containing one or more -O- or -S- atoms or -N(R<sup>11</sup>)-, -C(O) or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R<sup>3</sup> and R<sup>3a</sup>;

Alk<sup>4</sup> is a straight or branched C<sub>1-6</sub> alkylene, C<sub>2-6</sub> alkenylene or C<sub>2-6</sub> alkynylene chain, optionally interrupted by one, two, or three -O- or -S- atoms or -S(O)<sub>n</sub> or -N(R<sup>15</sup>)- groups;

R<sup>15</sup> is a hydrogen atom or C<sub>1-6</sub> alkyl group;

m is zero or an integer 1, 2 or 3;

n is an integer 1 or 2;

wherein the optional substituents for the aliphatic groups and the heteroaliphatic groups of R<sup>3a</sup> are selected from halogen atoms, hydroxy groups, C<sub>1-6</sub> alkoxy groups, thiol groups, C<sub>1-6</sub> alkylthio groups, amino groups, and substituted amino groups;

wherein the optional substituents for the cycloaliphatic, polycycloaliphatic, heterocycloaliphatic and heteropolycycloaliphatic groups of R<sup>3</sup> and R<sup>3a</sup> are selected from halogen atoms, C<sub>1-6</sub> alkyl groups, haloC<sub>1-6</sub> alkyl groups optionally substituted with hydroxyl groups, hydroxyl groups, C<sub>1-6</sub> alkoxy groups, haloC<sub>1-6</sub> alkoxy groups, thiol groups, C<sub>1-6</sub> alkylthio groups, aromatic groups, heteroaromatic groups, and -(Alk<sup>2</sup>)<sub>v</sub>R<sup>10</sup> groups;

Alk<sup>2</sup> is a straight or branched C<sub>1-3</sub> alkylene chain;

v is zero or an integer 1;

R<sup>10</sup> is a -OH, -SH, -N(R<sup>11</sup>)<sub>2</sub>, -CN, -CO<sub>2</sub>R<sup>11</sup>, -NO<sub>2</sub>, -CON(R<sup>11</sup>)<sub>2</sub>, -CSN(R<sup>11</sup>)<sub>2</sub>, -OC(O)N(R<sup>11</sup>)<sub>2</sub>, -C(O)H, -COR<sup>11</sup>, -OCO<sub>2</sub>R<sup>11</sup>, -OC(O)R<sup>11</sup>, -C(S)R<sup>11</sup>, -CSN(R<sup>11</sup>)<sub>2</sub>, -N(R<sup>11</sup>)COR<sup>11</sup>,



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EXAMINATION REPORT

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-N(R<sup>11</sup>)CSR<sup>11</sup>, -SO<sub>3</sub>H, -SOR<sup>11</sup>, -SO<sub>2</sub>R<sup>11</sup>, -SO<sub>3</sub>R<sup>11</sup>, -SO<sub>2</sub>N(R<sup>11</sup>)<sub>2</sub>, -N(R<sup>11</sup>)SO<sub>2</sub>R<sup>11</sup>,  
-N(R<sup>11</sup>)CON(R<sup>11</sup>)<sub>2</sub>, -N(R<sup>11</sup>)CSN(R<sup>11</sup>)<sub>2</sub>, or -N(R<sup>11</sup>)SO<sub>2</sub>N(R<sup>11</sup>)<sub>2</sub> group; and

R<sup>11</sup> is an atom or group as defined for R<sup>8</sup> or an optionally substituted cycloaliphatic or heterocycloaliphatic group as defined for R<sup>3</sup>;

and when R<sup>3</sup> is a heterocycloaliphatic group containing one or more nitrogen atoms each nitrogen atom is optionally substituted with a group -(L<sup>5</sup>)<sub>p</sub>(Alk<sup>3</sup>)<sub>q</sub>R<sup>12</sup>;

L<sup>5</sup> is -C(O)-, -C(O)O-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -CON(R<sup>11</sup>)-, -CSN(R<sup>11</sup>)-,  
-SON(R<sup>11</sup>)- or -SO<sub>2</sub>N(R<sup>11</sup>)-;

p is zero or an integer 1;

Alk<sup>3</sup> is an optionally substituted aliphatic or heteroaliphatic chain;

q is zero or an integer 1;

R<sup>12</sup> is a hydrogen atom or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group;

R<sup>a</sup> and R<sup>a'</sup>, which may be the same or different, are each independently selected from a hydrogen or halogen atom or an optionally substituted straight or branched alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkoxy, alkylthio or -(Alk<sup>b</sup>)<sub>m</sub>R<sup>b</sup> group (in which Alk<sup>b</sup> is a C<sub>1-3</sub> alkylene chain, m is zero or the integer 1, and R<sup>b</sup> is -OH, -SH, -NO<sub>2</sub>, -CN, -CO<sub>2</sub>H, -CO<sub>2</sub>R<sup>c</sup> (where R<sup>c</sup> is an optionally substituted straight or branched C<sub>1-6</sub> alkyl group), -SO<sub>3</sub>H, -SOR<sup>c</sup>, -SO<sub>2</sub>R<sup>c</sup>, -SO<sub>3</sub>R<sup>c</sup>, -OCO<sub>2</sub>R<sup>c</sup>, -C(O)H, -C(O)R<sup>c</sup>, -OC(O)R<sup>c</sup>, -C(S)R<sup>c</sup>, -NR<sup>d</sup>R<sup>e</sup> (where R<sup>d</sup> and R<sup>e</sup>, which may

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EXPEDITED PROCESSING

EXAMINING GROUP 1688

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 be the same or different, are each a hydrogen atom or an optionally substituted straight or branched C<sub>1-6</sub> alkyl group), -CON(R<sup>d</sup>)(R<sup>e</sup>), -OC(O)N(R<sup>d</sup>)(R<sup>e</sup>), -N(R<sup>d</sup>)C(O)R<sup>e</sup>, -CSN(R<sup>d</sup>)(R<sup>e</sup>), -N(R<sup>d</sup>)C(S)R<sup>e</sup>, -S(O)<sub>2</sub>N(R<sup>d</sup>)(R<sup>e</sup>), -N(R<sup>d</sup>)SO<sub>2</sub>R<sup>e</sup>, -N(R<sup>d</sup>)CON(R<sup>e</sup>)(R<sup>f</sup>) (where R<sup>f</sup> is a hydrogen atom or an optionally substituted straight or branched C<sub>1-6</sub> alkyl group), -N(R<sup>d</sup>)C(S)N(R<sup>e</sup>)(R<sup>f</sup>) or -N(R<sup>d</sup>)SO<sub>2</sub>N(R<sup>e</sup>)(R<sup>f</sup>) group);

Alk<sup>a</sup> is an optionally substituted C<sub>1-6</sub> aliphatic or C<sub>1-6</sub> heteroaliphatic chain containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>8</sup>)-, -C(O)NR<sup>8</sup>-, -OC(O)N(R<sup>8</sup>)-, -CSN(R<sup>8</sup>)-, -N(R<sup>8</sup>)CO-, -N(R<sup>8</sup>)C(O)O-, -N(R<sup>8</sup>)CS-, -S(O)<sub>2</sub>N(R<sup>8</sup>)-, -N(R<sup>8</sup>)S(O)<sub>2</sub>-, -N(R<sup>8</sup>)CON(R<sup>8</sup>)-, -N(R<sup>8</sup>)CSN(R<sup>8</sup>)-, and -N(R<sup>8</sup>)SO<sub>2</sub>N(R<sup>8</sup>)-;

wherein the optional substituents for the aliphatic and heteroaliphatic groups of Alk<sup>a</sup> are selected from halogen atoms, hydroxy groups, C<sub>1-6</sub>alkoxy groups, thiol groups, C<sub>1-6</sub>alkylthio groups, amino groups, and substituted amino groups;

r is zero or the integer 1;

R is a carboxylic acid (CO<sub>2</sub>H), a carboxylic ester group, or carboxylic amide group;

and the salts, hydrates and N-oxides thereof.

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 17. (Twice amended) A method for the treatment of a mammal suffering from inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma or